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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
07/13/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/821,568	REMACLE ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *1-26 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *27-33 and 35-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Applicants' response of April 27, 2007, to the non-final action dated December 15, 2006 has been entered. Claims 1-41 are pending in the application. Claims 27, 28, 30, 33 and 36-38 have been amended and claims 39-41 are newly added. No claims have been cancelled. Claims 1-26 and 34 remain withdrawn from consideration, without traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Claims 27-33 and 35-41 are currently under examination.

Response to Priority

Acknowledgment is made of Applicants' claim for foreign priority based on an application filed in the European Patent Office on 03/24/2000. Applicants' are correct in their assertion that a certified copy of the 00870057.7 NO application was filed in accordance with 35 U.S.C. 119(b), in the parent 09/816,763 application.

Response to Objections to the Specification/Abstract

The Abstract of the disclosure was objected to in the previous office action dated December 15, 2006, for referring to various elements using numbers. In view of Applicants' amendment to the Abstract removing reference numbers, the previous objection is hereby withdrawn.

Response to Claim Rejections - 35 USC § 112- Second Paragraph

Claims 27-33 and 35-38 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the previous office action dated December 15, 2006. Applicants' amendments of claims 27 and 36, canceling the limitation of "and possibly a second labeled antibody", deleting reference numbers in claim 27, and specifying that a 6.8 nm spacer is formed between the specific nucleotide sequence and the surface of the solid support, obviate the grounds for rejection. Thus, the previous rejection of the claims is hereby withdrawn.

New Claim Rejections - 35 USC § 112- Second Paragraph

Applicants' claim amendments have necessitated the following new grounds of rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim39, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Response to Claim Rejections - 35 USC § 103

Claims 27-29, 31-33 and 36-38 were rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, filed Apr. 29, 1994) in view of Hibma et al. (Nucl. Acids Res. 22:3806-3807; 1994); and claims 27, 30 and 35 were rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, filed Apr. 29, 1994), as applied to claims 27, 29, 31-33 and 36-38, in view of Church et al. (U.S. Patent No. 6,326,489, filed Aug. 5, 1997), in the previous office action dated December 15, 2006. In view of Applicants' arguments regarding the absence of a teaching in the cited references for detection of only activated forms of transcription factors, the previous rejections are hereby withdrawn.

However, the claims are subject to new rejections over the prior art, as set forth below.

New Claim Rejections - 35 USC § 103

Claims 27-29, 31-33 and 36-38 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, filed Apr. 29, 1994; of record) in view of Hibma et al. (Nucl. Acids Res. 22:3806-3807; 1994; of record), and further in view of Kaltschmidt et al. (Biol. Chem. Hoppe-Seyler 376:9-16; 1995).

A "kit" *per se* is not afforded any patentable weight, thus the instant claims are examined with respect to the elements and compositions contained in said kit.

Peterson et al. disclose a method comprising the steps of: a) binding to a solid substrate such as microtiter plate (column 5, line 34-36; column 7, line 23; column 8, lines 59-60), double-stranded DNA sequences (column 6, lines 26-28), at the concentration greater than 0.01 pmoles/cm^2 (column 10, line 26), wherein said double-stranded DNA is connected to the surface of the solid support via avidin-biotin binding (column 7, lines 13-18) or antigen/antibody binding (column 7, lines 18-19); b) contacting transcriptional factors with said solid-surface bound double-stranded DNAs (column 3, lines 1-5; column 4, lines 37-41); and c) identifying and/or quantifying a signal resulting from the binding of the transcriptional factors to said solid-surface bound double-stranded DNAs (column 8, lines 64-68). Thus, the preceding steps encompass a composition comprising the elements of the instantly claimed "kit". The authors disclose numerous transcription factor binding sequences in columns 3-5, comprising many of the members listed in table 1 of the instant application.

Peterson et al. describe the double-stranded DNA as a nucleic acid receptor coupled to a ligand, a candidate pharmacological agent and a receptor immobilized on a solid substrate that may be a filter, and the nucleic acid has at least that portion of a nucleotide sequence naturally involved in the regulation of the transcription of the gene which is necessary for sequence-specific interaction with the transcription factor (Abstract). The nucleic acid may be any length amenable to the assay conditions and requirements and may be preferably between 18 bp and 250 bp (column 6, lines 35-38), thus addressing the limitation of at least 6.8 nm length for the spacer region. While Peterson et al. do not refer to the double stranded oligonucleotide as having a spacer, they state that the nucleic acid contains at least a portion of which is common to the gene regulatory region to which the transcription factor normally binds, the binding site portion constituting between 4 and 8 nucleotides (column 6, lines 39-48). Thus, the remaining sequence length would constitute a spacer sequence.

The teachings of Peterson et al. are directed to drug screening assays and the detection of any sequence-specifically bound transcription factor (Abstract), pertinent to the binding of activated forms of transcription factors; the authors specifically describing the protocol for NF-kB p65/p50 binding assay (columns 12 and 13). Peterson et al. do not teach the detection of the

bound transcription factor by a first and second antibodies conjugated with an enzyme such as peroxidase, but state that the label which is used to detect protein-nucleic acid complexes may be for indirect detection such as an epitope tag, an enzyme, etc. (column 6, lines 7-14).

Hibma et al. describe a non-radioactive assay for the detection and quantitation of a DNA binding protein using an ELISA assay, that can be easily adapted for application to any known DNA binding protein for which antibodies are available (first column, p. 3806). Using double-stranded biotinylated oligonucleotides attached to streptavidin coated plates, the authors describe the use of a mouse monoclonal antibody to detect the HPV E2 protein in their assay using a peroxidase labeled anti-mouse polyclonal antibody (second column, p. 3806).

While neither Peterson et al. nor Hibma et al. describe an antibody specific for the activated form of a transcription factor, Kaltschmidt et al. describe a monoclonal antibody that selectively recognizes the activated form of the p65 NF-kB transcription factor in cultured cells (Title and Abstract). The monoclonal antibody is described as recognizing p65 in the nucleus but not the cytoplasm (first column, p. 10) and its specificity in total cell extracts is demonstrated in Fig. 1 (p. 10). Kaltschmidt et al. state that the antibody can be used to investigate the effectiveness of novel anti-inflammatory drugs in disease states by monitoring the downregulation of NF-kB *in vivo* (first column, p. 15).

Therefore, a person of ordinary skill in the art would have been motivated to include the NF-kB monoclonal antibody of Kaltschmidt et al. in the labeled antibody detection method of Hibma et al. with the NF-kB transcription factor binding method of Peterson et al., to quantify transcription factor binding to double stranded oligonucleotides immobilized on a solid surface. A person of ordinary skill in the art, having combined the antibody detection method of Hibma et al. with the anti p65 monoclonal antibody for detecting and quantifying NF-kB activated transcription factor binding, with the method of Peterson et al., would be able to practice the use of the instantly claimed kit to detect and quantify any activated DNA-binding transcription factor, utilizing the composition of the instantly claimed invention, with a reasonable expectation of success.

Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine the product elements of Peterson et al. with the labeled antibodies of Hibma et al.,

wherein the antibody is specific to the activated form of NF-kB, as described by Kaltschmidt et al., at the time of the instant invention.

Claims 27, 30 and 35 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Peterson et al. (U.S. Patent No. 5,563,036, filed Apr. 29, 1994), in view of Hibma et al. (Nucl. Acids Res. 22:3806-3807; 1994), and further in view of Kaltschmidt et al. (Biol. Chem. Hoppe-Seyler 376:9-16; 1995), as applied to claims 27-29, 31-33 and 36-38 above, in view of Church et al. (U.S. Patent No. 6,326,489, filed Aug. 5, 1997; of record).

Peterson et al. do not teach that the solid-support be an array bearing at least 4 spots/cm^2 of solid support surface, to be used as a high-throughput screening device, but state that the methods are particularly suited to automated high throughput drug screening (column 9, lines 15-16). Church et al. describe surface bound double-stranded DNA oligonucleotide arrays for use in rapid, high-throughput screening of compounds, that bind or otherwise interact with short, double-stranded DNA sequence motifs that bind transcription factors (column 1, first paragraph). Church et al. state that the array may have virtually any number of different members and a preferred array comprises from 2 up to 1,000 members per cm^2 (column 2, lines 37-45).

Therefore, a person of ordinary skill in the art would have been motivated to combine the high throughput screening method of Church et al. with the transcription factor binding method of Peterson et al., to quantify transcription factor binding and screen compounds directed to double stranded oligonucleotides immobilized on a solid surface. A person of ordinary skill in the art, having combined the high throughput screening method of Church et al., with the transcription factor binding and detection method, as taught by Peterson et al., Hibma et al. and Kaltschmidt et al. would be able to practice the screening, detection and quantification of activated transcription factors, utilizing the composition of the instantly claimed invention, with a reasonable expectation of success.

Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine the product elements of Peterson et al., Hibma et al. and Kaltschmidt et al., with the arrays described by Church et al. at the time of the instant invention.

Conclusion

Claims 27-33 and 35-41 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00-4:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on **(571) 272-0739**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

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